

**REMARKS**

In view of the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 1, 3, and 4 under 35 U.S.C. § 102(a) as anticipated by WO 96/15271 to Carrino (“Carrino”) is respectfully traversed.

As demonstrated by the accompanying Declaration of Francis Barany, Matthew Lubin, George Barany, and Robert P. Hammer under 37 C.F.R. § 1.131 (“Barany et al. Declaration”), Carrino is not prior art, because applicants made their invention prior to the May 23, 1996, International publication date of Carrino.

In particular, prior to June 22, 1994, applicants conceived, in the United States, the invention claimed in the above-identified patent application, and diligently reduced it to practice (Barany et al. Declaration ¶ 2). Evidence of this conception prior to June 22, 1994, is provided in Exhibit 1 (Id.). Exhibit 1 is a true copy of pages from Francis Barany, Ph.D.’s grant proposal to the U.S. Department of Health and Human Services, prepared prior to June 22, 1994, which discloses the development of a multiplex ligase detection reaction/polymerase chain reaction (LDR/PCR) system (Barany et al. Declaration ¶ 3). Exhibit 1 also teaches the design of LDR primers for the detection of tumor genes; all of these primers have common artificial PCR primer sequences to allow subsequent amplification using only two PCR primers (Id.). This LDR/PCR system is illustrated in Figure 15 of Exhibit 1 (Id.). In particular, Figure 15 illustrates the quantification of gene amplifications and deletions using LDR/PCR as follows (Id.). A sample containing a plurality of DNA templates is denatured at 94°C (Id.). The LDR primers are added, allowed to anneal to complementary sequences on the DNA templates, and ligated with a thermostable ligase (Id.). A DNA polymerase is added and PCR is carried out to amplify all LDR products simultaneously using two common “zip code” primers (Id.). As shown in Figure 15, the zip code primers are labeled to allow for detection of the extension products following PCR (Id.). Detection is carried out either by separation and quantification of different sized labeled ligation products or by capture on the appropriate oligonucleotide or PNA addressable array (Id.).

Under 35 U.S.C. § 102(a), a person is entitled to a patent unless “. . . the invention was. . . described in a printed publication in this or a foreign country before the invention thereof by the applicant for patent.” Since the May 23, 1996, International

publication date of Carrino is after applicants' date of invention, which was prior to June 22, 1994, Carrino cannot be prior art under 35 U.S.C. § 102. Accordingly, the rejection based on Carrino should be withdrawn.

The rejection of claims 1, 3, and 4 under 35 U.S.C. § 102(a) as anticipated by WO 95/35390 to Zhang et al. ("Zhang '390") is respectfully traversed.

Zhang '390 has a publication date of December 28, 1995. Since this date is after applicants' date of invention, as demonstrated in the Barany et al. Declaration, Zhang '390 is not prior art under 35 U.S.C. § 102. Accordingly, the rejection based on Zhang '390 should be withdrawn.

The rejection of claims 1, 3, and 4 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,876,924 to Zhang et al. ("Zhang '924") is respectfully traversed.

Under 35 U.S.C. § 102(e), a person is entitled to a patent unless "the invention was described in . . . (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent . . ." The earliest effective filing date of Zhang '924 is June 22, 1994. Since this is after applicants' date of invention, Zhang '924 cannot be prior art under 38 U.S.C. § 102. Accordingly, the rejection based on Zhang '924 should be withdrawn.

The rejection of claims 2, 5-9, and 64-70 under 35 U.S.C. § 103(a) for obviousness over any one of Carrino, Zhang '390, or Zhang '924 is respectfully traversed. Since Carrino, Zhang '390, and Zhang '924 are not available as prior art, the obviousness rejection over any one of Carrino, Zhang '390, or Zhang '924 must be withdrawn.

The rejection of claims 59-63 under 35 U.S.C. § 103(a) for obviousness over any one of Carrino, Zhang '390, or Zhang '924 in view of U.S. Patent No. 5,418,149 to Gelfand et al. ("Gelfand") is respectfully traversed.

It is the position of the U.S. Patent and Trademark Office that it would have been obvious to use dUTP and uracil N-glycosylase in the method of any of Carrino, Zhang '390, or Zhang '924 to make the present invention. However, as discussed above, Carrino, Zhang '390, and Zhang '924 are not prior art. Furthermore, Gelfand does not teach or suggest the claimed combination of LDR and PCR to identify one or more different nucleotide sequences in a sample. Accordingly, the rejection of claims 59-63 under 35 U.S.C. § 103(a) for obviousness over any one of Carrino, Zhang '390, or Zhang '924 in view of Gelfand is improper and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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